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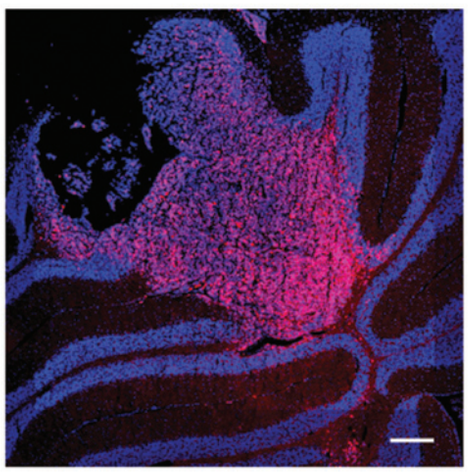
CLINICAL CANCER RESEARCH HIGHLIGHTS

Selected Articles from This Issue

OLIG2 is a Therapeutic Target for *MYC*-Amplified Medulloblastoma



Xu *et al.* | Page 4278

Patients with *MYC*-amplified medulloblastoma (MB) have poor prognosis and frequently develop recurrence; thus new therapeutic approaches to prevent recurrence are needed. Here, Xu and colleagues demonstrate that OLIG2-expressing tumor cells are highly enriched in therapy resistant and recurrent *MYC*-amplified MB and high levels of OLIG2 correlated with poor prognosis. Genetic or pharmacological inhibition of OLIG2 in combination with radiotherapy significantly suppressed the progression of OLIG2-high tumors in patient-derived xenograft mouse models, indicating that OLIG2 represents a novel therapeutic target in high-risk MB. CT-179 is a highly potent and selective small molecule OLIG2 inhibitor. The study provides evidence for CT-179 to potentially act as an adjunctive therapy for patients with high-risk MB as well as other types of pediatric brain tumors where OLIG2 is highly expressed. Thus patients with these cancers may also benefit from CT-179 treatment.

Circulating TTMV-HPV DNA Detection of Occult Recurrent OPSCC

Berger *et al.* | Page 4292

Cell-free tumor tissue modified viral (TTMV)-HPV DNA is a unique biomarker, present in blood of patients with HPV-driven malignancy, distinct from HPV DNA from HPV infection. To assess real-world usage of TTMV-HPV DNA for the surveillance of patients with HPV-driven oropharyngeal squamous cell carcinoma (OPSCC), Berger and colleagues conducted a multisite, retrospective clinical case series of >1,000 patients. TTMV-HPV DNA demonstrated 95% positive and 95% negative predictive value for recurrent OPSCC and was commonly the first indication of recurrence among asymptomatic individuals. These data may inform and expand future clinical and guideline-endorsed strategies for HPV-driven malignant disease surveillance.

MLH1 Promoter Hypermethylated Endometrial Cancer

Manning-Geist *et al.* | Page 4302

DNA mismatch repair (MMR)-deficiency (MMR-D) is present in 20-40% of endometrial carcinomas (ECs) and is driven by epigenetic *MLH1* promoter hypermethylation (*MLH1*ph) or somatic or germline genetic alterations in MMR genes. Manning-Geist and colleagues examined EC with paired tumor-normal testing and found that *MLH1*ph ECs exhibited a lower tumor mutational burden, fewer tumor infiltrating lymphocytes, and distinct somatic mutational profiles compared with EC harboring germline or somatic MMR mutations. Patients with *MLH1*ph EC also had shorter time to progression, suggesting that subclassification of MMR-deficient EC is warranted given the distinct clinicopathologic, molecular, and immunologic profiles of *MLH1*ph EC.

Clinicopathological and Molecular Subtyping of EGFR Mutation

Jung *et al.* | Page 4312

To identify risk factors for recurrence-free survival (RFS) in early-stage EGFR mutation-positive NSCLC after curative intent surgery, Jung and colleagues performed analysis of clinicopathological data of 1,181 patients and molecular data of 56 patients with matched case-controls (stage and type of EGFR mutation). This comprehensive analysis shows TP53 mutation, RNA subtype (non-TRU), and clinicopathological risk factors (micropapillary subtype, vascular invasion, pleural invasion) were associated with poor RFS independent of pathological stage. This study highlights that patients with early-stage EGFR-mutation-positive NSCLC had diverse outcomes depending on clinicopathological risk factors, concurrent molecular alterations, and RNA subtype and need personalized adjuvant treatment.

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